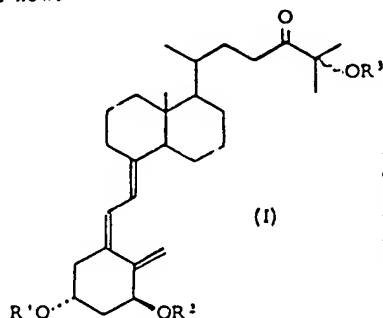


50771 D/28 B05 (B01) TEIJ 26.10.79
TEIJIN KK *J56061-351
26.10.79-JP-137771 (26.05.81) A61k-31/59 C07c-172
1-Alpha, 25-dihydroxy-24-oxo:cholecalciferol deriva -
exhibit vitamin/D 3 pharmacological activities. prepd. from
24-oxo-cholesta-5,7-diene cpds.

1a, 25-Dihydroxy-24-oxocholecalciferols of formula (I)
are new:



(R¹, R² and R³ = H
or hydroxy protecting
gp. (pref. 1-12C ali-
phatic or aromatic
acyl, trialkylsilyl, 2-
tetrahydropyranyl, or
2-tetrahydrofuranyl)).

B(1-D2, 3-G). 2

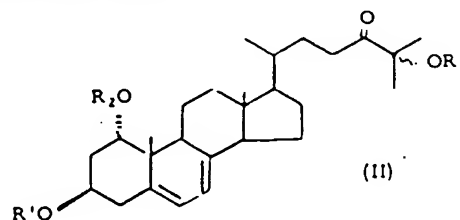
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USE/ADVANTAGE

(I) exhibit vitamin D₃-like pharmacological activities.
On reduction of the 24-oxo, (I) are converted into 1a, 24,
25-trihydroxyvitamin D₃ as active vitamin D₃.

PREPARATION

(I) are prepd. by irradiating 1a, 25-dihydroxy-24-oxo-
cholesta-5,7-dienes (II) with ultraviolet rays to yield 1a, 25-
dihydroxy-24-oxoprevitamins D₃, isomerising the latter
with thermal energy, if required followed by removal of the
hydroxy protecting gp.



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The UV rays pref. have wavelength 200-360 nm, esp. 260-
310 nm. The reaction is conducted in an inert solvent-
including hydrocarbons and haloalkanes (e.g. hexane,
heptane, PhH, PhMe, xylene, PhCl), ethers (e.g. Et₂O, THF,
dioxane), and alcohols (e.g. MeOH, EtOH, PrOH) at a temp.
of -20°C to 120°C, pref. -10°C to 50°C. The subsequent
thermal isomerisation is carried out at 20-120°C, pref.
40-100°C in the inert solvent.

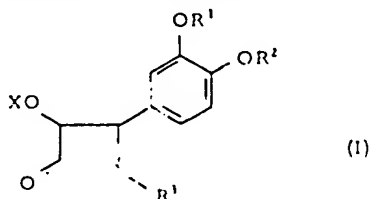
EXAMPLE

A soln. of 70 mg 1a, 3β, 25-trihydroxy-24-oxocholesta-5,7-
diene dissolved in a mixt. of 50 mg deoxygenated EtOH and
500 ml Et₂O was irradiated with a 200W lamp surrounded by
a Vycor filter at 10-20°C with stirring for 6 hrs. The
cold soln. was evapd. in vacuo at 30°C, and the residue was
dissolved in 250 ml deoxygenated PhH and refluxed under
heating for 2.5 hr. After the reaction completion, the mixt.
was evapd. in vacuo, and the resulting residue was chrom-
atographed on a thin layer of silica gel preliminarily treat-
ed with 2% AgNO₃-MeCN (solvent: CHCl₃-MeOH) and of sil-
ica gel (PhH-Me₂CO) to give 10.8 mg 1a, 25-dihydroxy-24-
oxovitamin D₃, mp. 91-93.5°C. (6ppW52)

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50772 D/28 B03 SAGA 24.10.79
SAGAMI CHEM RES CENTRE *J56061-352
24.10.79-JP-134485 (26.05.81) C07c-101/77 C07d-205/08
3-Hydroxy-beta-lactam cpds. can be prepd. economically -
and are used in DOPA prepn. used in antiparkinson
treatment.

3-Hydroxy-β-lactam cpds. of formula (I) are new:



(R¹ and R² = H, lower alkyl, benzyl or acyl, or R¹ and R²
taken together may form alkylene;
R¹ = alkyl, aryl or heteroaromatic gp.;
X = H, benzyl or tosyl).

USE/ADVANTAGE

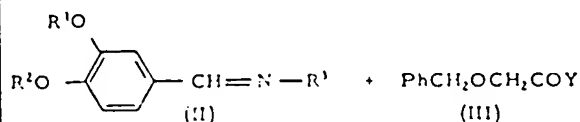
(I) can be converted into DOPA (useful as antiparkinson-

B(6-A2, 7-D1). 2

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ism agent) on reaction with NaN₃, cleavage of the β-lactam
ring, and acid treatment. (I) can be prepd. from cheap
raw material.

PREPARATION



step (A) → (I) (X = benzyl) → step (B) → (I) (X = H)
→ step (C) → (I) (X = tosyl)

(Y is not defined but probably halogen).

Step (A) is carried out in a solvent, e.g. PhH, PhMe, THF,
CH₂Cl₂, in presence of a tert. amine, e.g. Et₃N, Pr₃N,
Bu₃N, pyridine, N-methylpiperidine, N-methylpyrrolidine
DBU, at -78°C to 100°C.

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Step (B) comprises hydrogenolysis with Pd catalyst (e.g. Pd black, Pd-C) in a solvent (e.g. MeOH, EtOH, CH₂Cl₂, CHCl₃, PhH, PhMe, THF, MeCN, DMF) at room temp. to 150°C, pref. 50-100°C.

Step (C) comprises tosylation with p-TsCl in presence of a tert-amine in an aprotic solvent (e.g. CH₂Cl₂, CHCl₃, PhH, PhMe, THF, MeCN, Me₂CO, DMF, DMSO) at -30°C to 100°C.

EXAMPLE

To a soln. of 5.00 g 3,4-dimethoxybenzylideneaniline and 2.50 g Et₃N in 50 ml PhH was dropwise added slowly a soln. of 4.60 g benzyloxyacetyl chloride in 50 ml PhH under ice cooling. The reaction mixt. was gradually warmed up to room temp., stirred for 15 hrs., washed with water, dried on MgSO₄, and evapd. in vacuo to give 8.18 g light yellow oil. This was chromatographed on silica gel and eluted with n-hexane-EtOAc (4:1) to give 4.16 g cis-isomer of 1-phenyl-3-benzyloxy-4-(3,4-dimethoxyphenyl)azetidin-2-one as white crystals, m. pt. 130-133°C, and 2.38 g trans-isomer as a colourless oil, n_D²⁰: 1.6018, (10ppW52).

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50774 D/28

B03 C02 E13

MITU 23.10.79

MITSUBISHI CHEM IND KK

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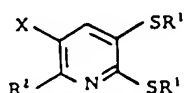
23.10.79-JP.136740 (26.05.81) C07d:211/90 C07d:213/80

Nicotinic acid derivs. - used as agrochemicals, drugs and chemical intermediates

BC(7-D4)E(7-D4)N(5-A). 1

1 1 1

Nicotinic acid derivs. of formula (I) are new:



(I)

(R¹ = lower alkyl (e.g. Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu);

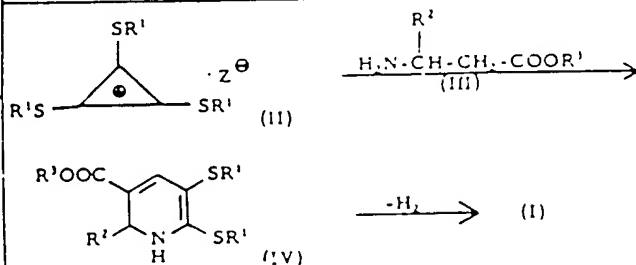
R² = H, lower alkyl or aryl (e.g. phenyl, tolyl);

X = lower alkoxycarbonyl (e.g. MeOCO-, EtOCO-, n-PrOCO-, i-PrOCO-) or COOH).

USE

(I) are utilized as agrochemicals or drugs or as raw material in production of various chemicals. (I) can be converted into nicotinic acid or its esters by removal of -SR¹ on hydrogenolysis with Raney Ni catalyst.

PREPARATION



(Z⁻ = anion (e.g. halogen ion, ClO₄⁻, BF₄⁻, SbF₆⁻, SbCl₆⁻, AlCl₄⁻);
R³ = lower alkyl).

DETAILS

(II) has been described in J48096564.

The reaction is carried out in a solvent, e.g. CH₂Cl₂, CHCl₃, dimethoxyethane, DMF, MeOH, pref. in presence of a base, e.g. NaH, t-BuOK, at -100°C to the reflux temp. of

J56061354

the solvent used, pref. room temp. to 100°C, for a period of 0.1-10 hrs., pref. 0.5-5 hrs.

The subsequent dehydration is achieved by allowing (IV) to stand in a halogenohydrocarbon solvent, e.g. CHCl₃, CCl₄, fluorohydrocarbon, perfluorohydrocarbon, at 0°C to the reflux temp. of the solvent used, pref. room temp., for a period of 3-24 hrs., pref. 10-15 hrs.

EXAMPLE

A mixt. of tri-t-butylthiocyclopropenium perchlorate (1 mmole, 403 mg.) and methyl α-aminopropionate (2 mmole) in 40 ml. DMF is allowed to stand at 80°C in presence of NaH (3 mmole) for 1 hr. Water is added, and the mixt. is extracted with hexane. The extract is dried on Na₂SO₄ and evapd., the residue is chromatographed on silica gel to give methyl 2,3-di-t-butylthio-1,6-dihydronicotinate in 72% yield.

This is dissolved in 10 ml. CCl₄ and allowed to stand under air for 2 hrs. to give methyl 2,3-di-t-butylthio-nicotinate in quantitative yield. (5ppW52)

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